

### REMARKS

Favorable reconsideration of the above-identified application in view of the amendments above and the remarks following is respectfully requested.

Claims 1-113 are pending in the application, of which Claims 5-8, 10-12, 16, 17 and 22-113 have been withdrawn. Claims 1-4, 9, 13-15 and 18-21 have been rejected. Claims 2-3, 9, 18-21 have now been cancelled. Claims 1 and 4 have now been amended.

### *Specification*

The Examiner states that the specification references an incorrect table (Table V and not Table IV) in four places – Page 24, lines 22; page 25, line 5; page 47, line 5 and page 48, line 5.

Please note that the reference to Table V on page 24, line 22 is correct. This is verified by the term "also" on line 23, underlined in the paragraph below. In order to clarify that the markers which distinct between disease related and non-disease related T-cell myelin reactivity are in Table 4, please amend page 24, paragraph on line 22-29 as specified on Page 3:

*"Of particular importance is the marker set provided in Table V. As is described in the Examples section which follows, the present inventors also uncovered cellular markers which distinct between disease-related and non-disease related T-cell myelin reactivity. Although MS appears to be caused by autoimmune T-cells activated against myelin self-antigens, myelin-reactive T-cells have been demonstrated in healthy subjects as well. Thus, distinction between disease-related and non-disease related T-cell myelin reactivity is of great clinical and investigational importance".*

Please note that the reference to Table V on page 25, line 5 is also correct. This is verified by the sentence in the same paragraph which states:

*"This marker set accurately defines the requirements for an individual to develop MS, and thus has important predictive value, especially in diagnosing*

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*individuals having MS in the “probable” stage”.*

Please amend page 47, paragraph on lines 5-12 and page 48, paragraph on lines 4-13 as specified on Page 3:

The Examiner states that the brief description of the drawings of the specification refers to colors that cannot be seen in the black and white drawings.

Please find enclosed a petition to be filed under 37 CFR 1.84(a) (2) requesting permission to use color photographs.

Further, please add the paragraph specified on page 4 to page 14, line 29, which specifies that the drawings are executed in color.

The Examiner has objected to the disclosure for containing embedded hyperlinks. Please amend the specification as indicated on Pages 4 and 5.

The Examiner states that it is improper to incorporate subject matter by reference to GenBank Accession numbers. Please find enclosed a substitute specification which references each sequence by a sequence ID number. In addition, please find enclosed a disc containing a sequence listing for all the sequences. The material being inserted is the same material that was incorporated by reference in the original application. As such, the amendment contains no new matter.

The Examiner has objected to the use of non-capitalized trademarks and their use without accompaniment of their generic terminology. Please amend the specification as indicated on Pages 5-9.

### ***35 U.S.C. § 112, First Paragraph Rejections***

The Examiner has rejected Claims 1-4, 9, 13-15 and 18-21 under 35 U.S.C. § 112, first paragraph for not providing sufficient enablement to the claims.

The Examiner states that the complex matter of the subject matter of this invention requires narrower claims. The Examiner then proceeds to exemplify the broad nature of the claims. Specifically, the Examiner states that the claims encompass any sample. The Examiner further maintains that the claims may be read

as determining one, or more than 1200 genes, or any number in-between. The Examiner further states that the claims also read upon any substantial difference between gene expression and not necessarily a statistically significant difference. The Examiner also maintains that the claims encompass any subject, whether human or animal. Further, the Examiner states that the claims encompass the use of any control individual.

The Examiner concludes that such broad claims are not enabled.

The Examiner's rejections are traversed. Notwithstanding, please note that the claims have now been limited to samples comprising peripheral blood mononuclear cells, **each of** the genes in Table I or II, human subjects, and the difference being a statistically significant difference. Applicant states that the method as claimed including testing **each of** the genes in Table I or II has sufficient predictability such that the number of controls need not be increased beyond a single control subject from a non-diseased subject.

Support for the phrase "sample comprising peripheral blood mononuclear cells" can be found in cancelled claim 3.

Support for the phrase "control sample of peripheral blood cells from a non-diseased subject" can be found throughout the instant specification - see for example page 33, lines 19-20.

Support for the term "human" may be found on page 45, lines 13-16.

Support for the phrase "statistically significant difference" may be found in claim 4.

The Examiner further states that the sequence of the genes are critical or essential to the practice of the invention and reference by a GENBANK number is not sufficient as incorporation of subject matter by reference to a hyperlink is considered to be an improper incorporation by reference.

In re Application of: Achiron et al  
Serial No.: 10/507,380  
Filed: July 18, 2005  
Office Action Mailing Date: February 20, 2008

Examiner: Duston, Jennifer Ann  
Group Art Unit: 1636  
Attorney Docket: 28594

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Please note that the sequences of all the claimed genes have now been provided – see enclosed disc for sequence listing. In addition, amended Tables are also enclosed such that it is possible to correlate the sequences of the sequence listing with a particular gene. As mentioned, addition of the sequences is the same material that was incorporated by reference and the amendment contains no new matter.

The Examiner further notes that the specification does not teach the use of the genes of Tables III-V to diagnose a subject with MS.

Examiner's objection is traversed. Notwithstanding, please note that Claim 1 has now been amended to limit the genes that can be used for diagnosis to those appearing in Tables I or II only.

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In view of the above amendments and remarks, it is respectfully submitted that claims 1, 4 and 13-15 are now in condition for allowance. An early Notice of Allowance is respectfully and earnestly solicited.

Respectfully submitted,



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Date: August 19, 2008

**Encls:**

- Petition for Extension (Three Months)
- Declaration in compliance with 37CFR 1.67(a).
- Sequence Listing Disc in CRF Copy
- Sequence Listing Disc in Written Compact Disc Format (2 Copies)
- Petition to File Color Drawings
- Annotated Marked-Up Specification
- Substitute Specification